UCLA Statistics

scReadSim: a Single-cell RNA-seq and ATAC-seq Read Simulator

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The Junction of Statistics and Biology
Department of Statistics
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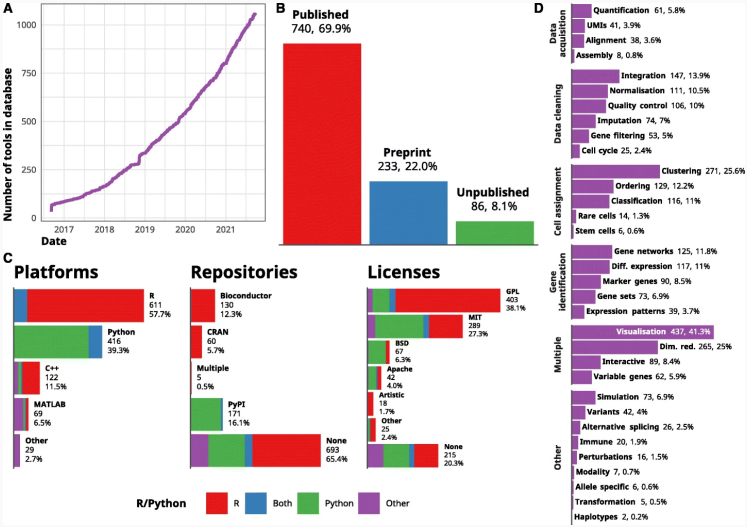
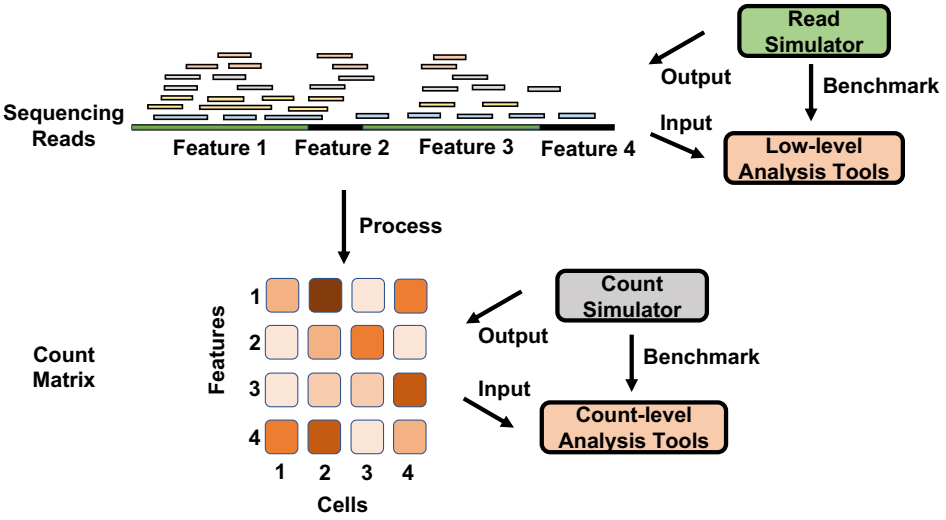
Over 1000 tools developed for single cell RNA-seq data



Luke Zappia and Fabian J Theis. Over 1000 tools reveal trends in the single-cell rna-seq analysis landscape. Genome biology, 22(1):1–18, 2021.

Analysis tools for single-cell sequencing technologies



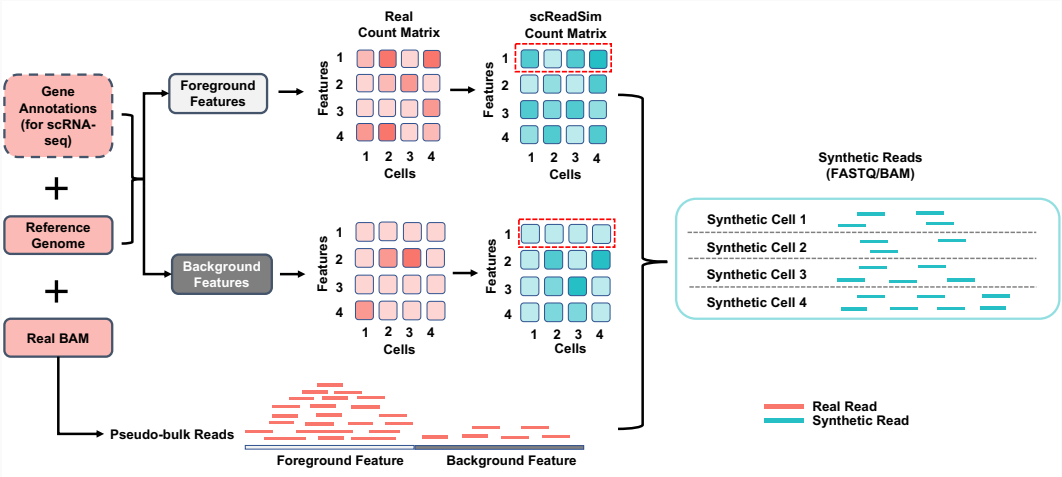
scReadSim

We here propose
scReadSim: a single-cell RNA-seq and ATAC-seq read simulator.

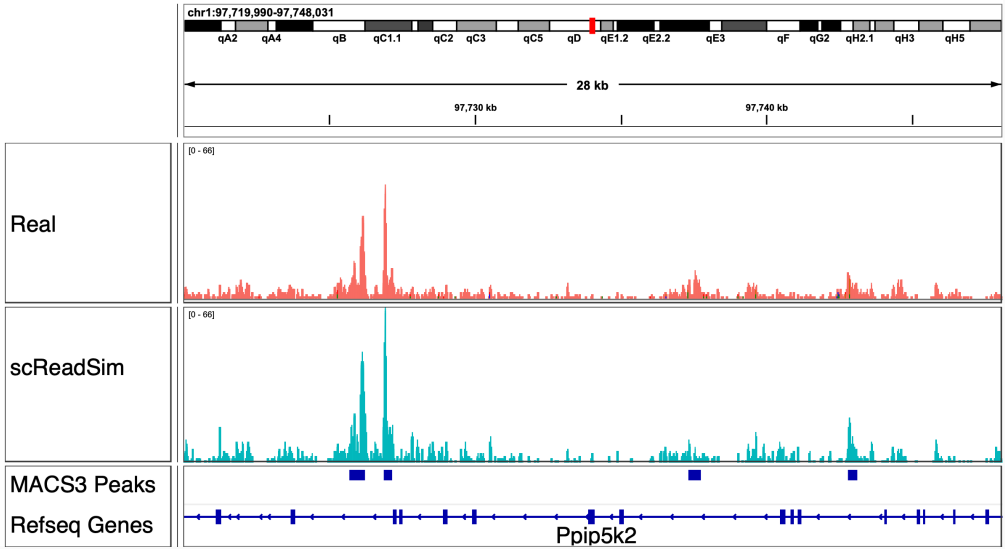
Advantages:

- aiming for **two omics data**: scRNA-seq and scATAC-seq
- simulating **realistic reads** for synthetic cells
- **flexibility**: varying cell
  number and sequence depth; user-specified peaks for scATAC-seq

Workflow for scReadSim



Verification: scReadSim synthetic cells mimics real cells in read level



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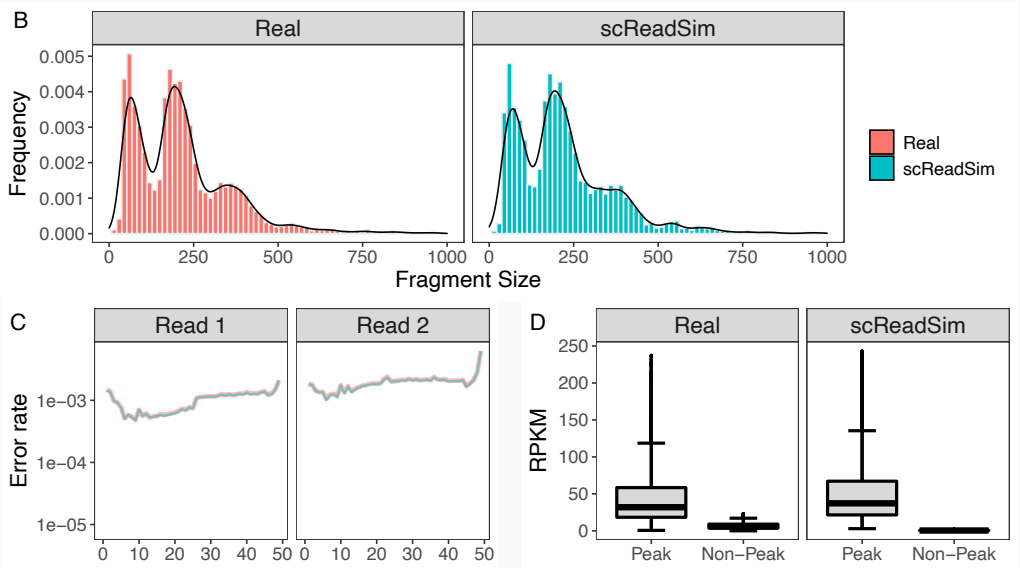
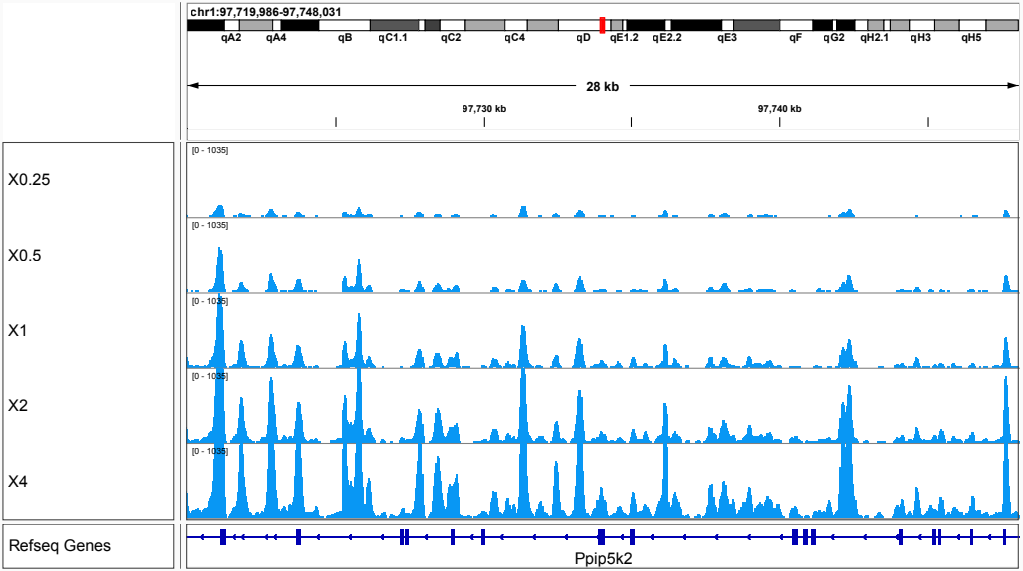
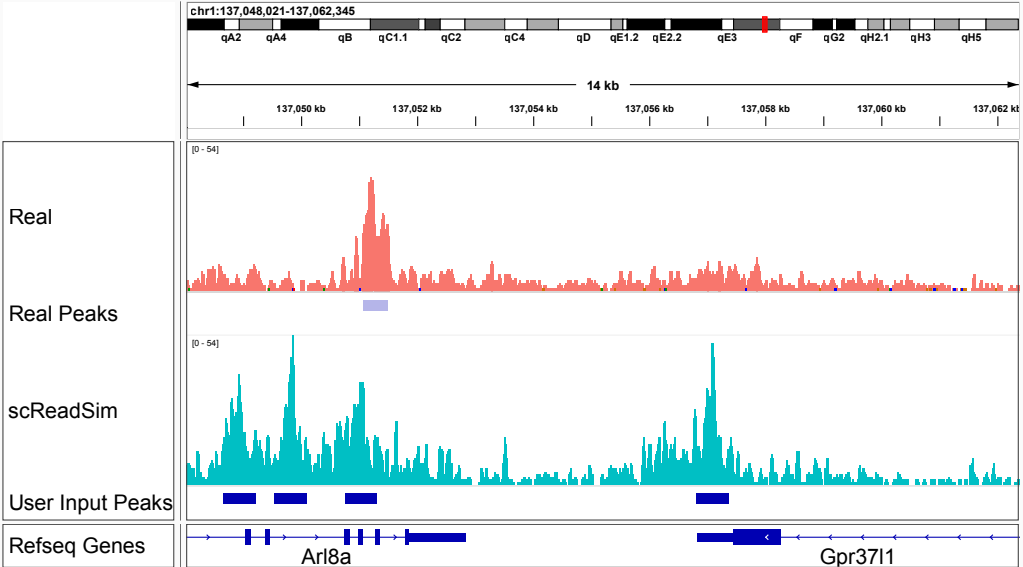


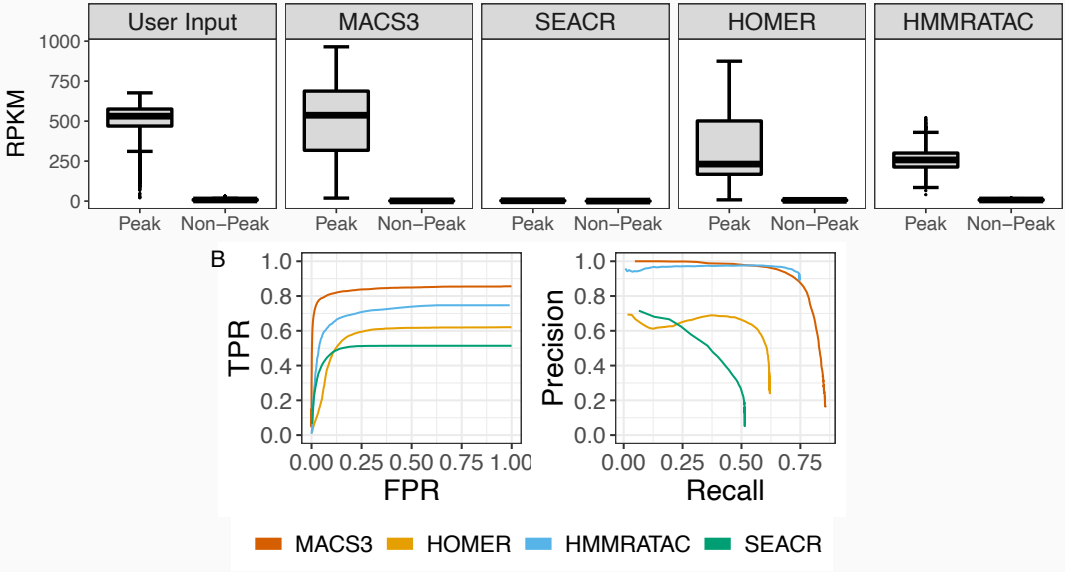
Flexibility: varying cell number and sequence depth



Flexibility: user-specified peaks for synthetic scATAC-seq data



Application: benchmark study of scATAC-seq peak calling methods



Materials

Preprint: Guanao Yan and Jingyi Jessica Li. "scReadSim: A Single-Cell Multi-Omics Read Simulator." bioRxiv. https://doi.org/10.1101/2022.05.29.493924.

Python package: http://screadsim.readthedocs.io/
Github page:
https://github.com/JSB-UCLA/scReadSim

Backup slides

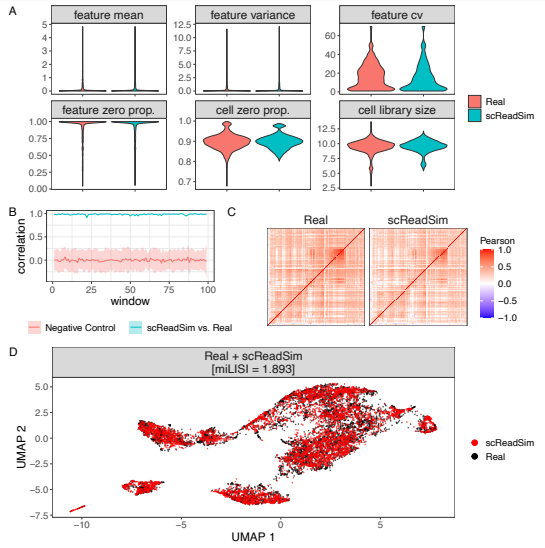
Verification 1: scReadSim synthetic cells mimics real cells in read level

- Read level
  - A. k-mer specturm
  - B. fragment length distribution
  - C. read error per base
  - D. Reads Per Kilobase Million (RPKM)
  - E. Read coverage comparison through the genome browser.
- Peak level
  - A. Venn diagram of peak calling results using MACS3 on both scReadSim synthetic and real BAM files.
  - B. True positive rate (TPR) vs. false positive rate (FPR) and false discovery rate (FDR) vs. TPR by taking real peaks as truths.
  - C. Read coverage comparison through the genome browser.

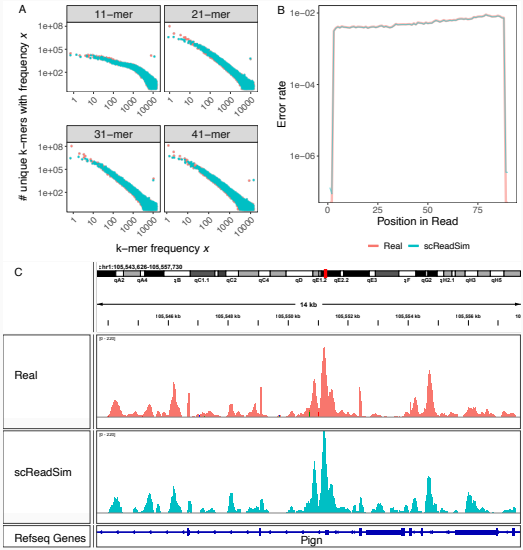
Verification 2: scReadSim synthetic cells mimics real cells in read count level

- Count level
  - A. Summary statistics: **Features (rows)** mean, variance, coefficient of variance, sparsity; **Cells (columns)** sparsity, library size.
  - B. Correlation between synthetic and real counts of windows. Each window include the same number of adjacent foreground features along the reference genome.
  - C. Correlation among top 100 expressed features.
  - D. Visualization of dimension reduction results using UMAP.

For B, we also include a control group: for each real window, we randomly select 100 real window from the remaining to calculate the correlation. The mean and standard deviation are shown as a contrast.

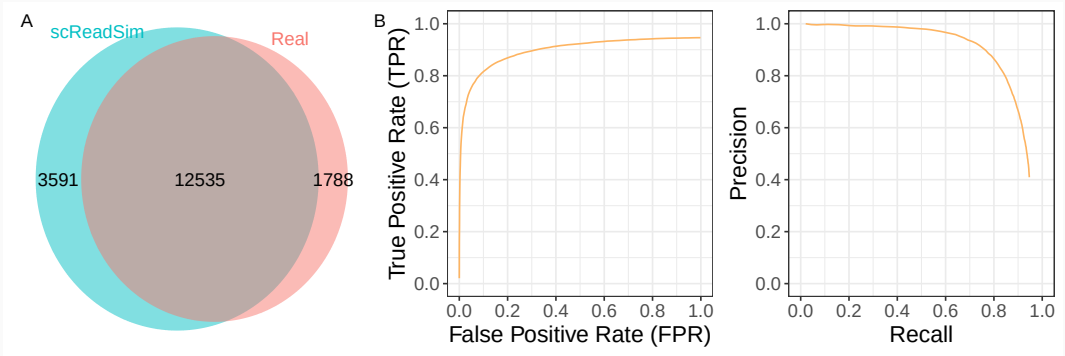


Synthetic reads generated by scReadSim resembles real 10x scRNA data in count level.

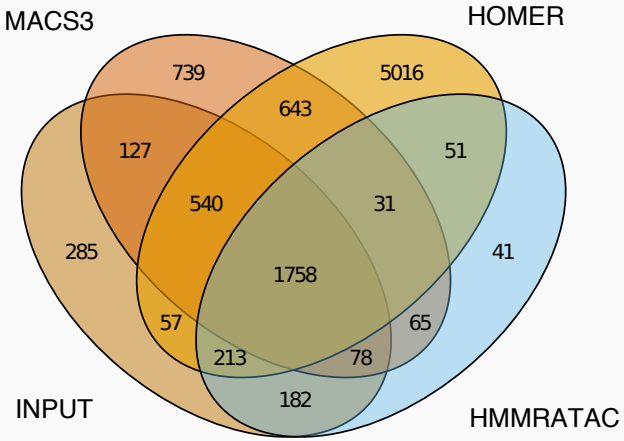


Synthetic reads generated by scReadSim resembles real 10x scRNA data in read level.

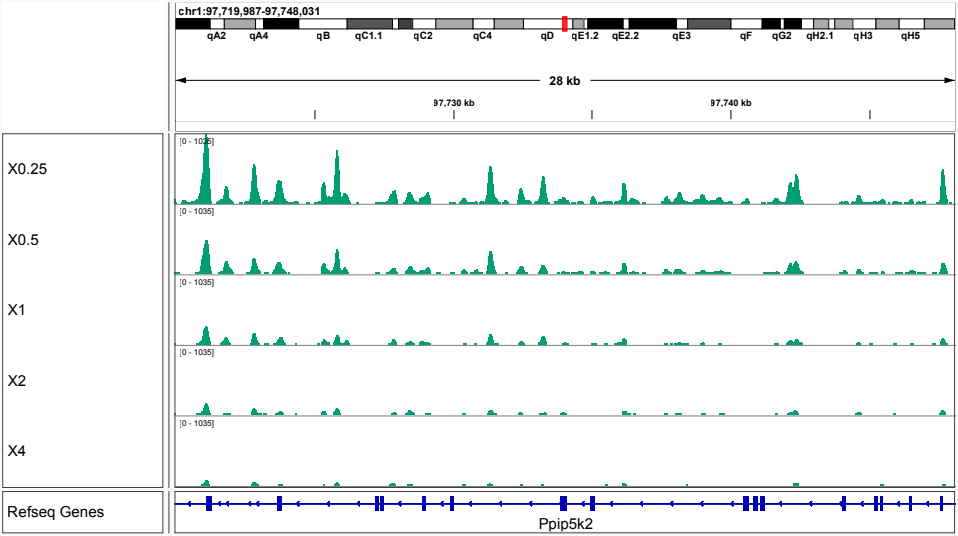
Verification: scReadSim synthetic cells mimics real cells in read level



Application 1: Benchmark study of peak calling methods



Flexibility: user-specified synthetic cell number and sequence depth



Application 2: benchmark of scRNA-seq deduplication methods